

CLAIMS

What is claimed is:

1. A method for treating sensorineural hearing loss comprising administering to a subject having a lesion in the inner ear a therapeutically effective amount of a neurturin protein product.
2. The method of claim 1, wherein the hearing loss is associated with injury or degeneration of neuroepithelial hair cells in the inner ear.
3. The method of claim 1, wherein the hearing loss is associated with injury or degeneration of spiral ganglion neurons.
4. The method of claim 1, wherein the neurturin protein product is the amino acid sequence set forth in Figure 1, 2, 4 or 5 (SEQ ID NOs: 1, 2, 3, 4 or 5) or a variant or a derivative thereof.
5. The method of claim 4, wherein the neurturin protein product has the amino acid sequence set forth in Figure 1 (SEQ ID NO: 1).
6. The method of claim 4, wherein the neurturin protein product has the amino acid sequence set forth in Figure 4 (SEQ ID NOs: 3 and 4).
7. The method of claim 4, wherein the neurturin protein product is [Met¹]neurturin.
8. The method of claim 1, wherein the neurturin protein product is administered at a dose of about 1 µg/kg/day to about 100 mg/kg/day.

09377446.081999

9. The method of claim 1, wherein the neurturin protein product is administered by cell therapy or gene therapy means wherein cells have been modified to produce and secrete the neurturin protein product.
10. The method of claim 8, wherein the cells have been modified *ex vivo*.
11. The method of claim 8, wherein the cells have been modified *in vivo*.
12. A method for treating lesions or disturbances to the vestibular apparatus comprising administering to a subject having such a lesion or disturbance a therapeutically effective amount of a neurturin protein product.
13. The method of claim 12, wherein the lesion or disturbance results in dizziness, vertigo or loss of balance.
14. The method of claim 12, wherein the neurturin protein product is the amino acid sequence set forth in Figure 1, 2, 4 or 5 (SEQ ID NO: 1, 2, 3, 4, or 5) or a variant or a derivative thereof.
15. The method of claim 14, wherein the neurturin protein product has the amino acid sequence set forth in Figure 1 (SEQ ID NO: 1).
16. The method of claim 14, wherein the neurturin protein product has the amino acid sequence set forth in Figure 4 (SEQ ID NOs: 3 or 4).
17. The method of claim 14, wherein the neurturin protein product is [Met⁻¹]neurturin.
18. The method of claim 12 wherein the neurturin protein product is administered at a dose of about 1 µg/kg/day to about 100 mg/kg/day.

09377446.081999

19. The method of claim 12, wherein the neurturin protein product is administered by cell therapy or gene therapy means wherein cells have been modified to produce and secrete the neurturin protein product.
20. The method of claim 19, wherein the cells have been modified *ex vivo*.
21. The method of claim 19, wherein the cells have been modified *in vivo*.

1 22. A neurturin protein product comprising the amino acid sequence depicted in Figure 4 (SEQ ID NOs: 3 or 4).

2 23. The protein of Claim 22, wherein the amino acid sequence has a methionine residue at the amino terminal.

3 24. The protein of Claim 22, which is modified by attachment of one or more polymeric moieties.

4 25. The protein of Claim 24, wherein the polymeric moiety is polyethylene glycol.

5 26. A pharmaceutical composition comprising a neurotrophic protein of claim 22, 1 in combination with a pharmaceutically suitable carrier.

6 27. A nucleic acid sequence encoding a neurturin protein product comprising the amino acid sequence depicted in Figure 4 (SEQ ID NOs: 3 or 4).

7 28. The nucleic acid sequence of claim 27, 6 comprising the sequence depicted in Figure 3 (SEQ ID NO: 3).

8 29. A vector comprising expression regulatory elements operatively linked to a nucleic acid sequence of claim 27. 6

9 30. A host cell transformed or transfected with the vector of claim 29. 8

- 10/31. The host cell of claim ⁹30 selected from the group consisting of mammalian cells and bacterial cells.
- 11/32. The host cell of Claim ⁹30, wherein said cell is suitable for human implantation and wherein said cell expresses and secretes said neurturin protein product.
- 12/33. The host cell of Claim ⁹30, wherein said cell is transformed or transfected *ex vivo*.
- 13/34. The host cell of Claim ⁹30, wherein said cell is enclosed in a semipermeable membrane suitable for human implantation.
- 14/35. A method for the production of a neurotrophic factor comprising the steps of:
- (a) culturing a host cell transformed or transfected with a nucleic acid sequence encoding a neurotrophic factor comprising the amino acid sequence depicted in Figure 4 (SEQ ID NOs: 3 or 4) under conditions suitable for the expression of said neurotrophic factor by said host cell; and
 - (b) optionally, isolating said neurotrophic factor expressed by said host cell.
- 15/36. The method of claim ¹⁴35, wherein said nucleic acid sequence comprises the sequence depicted in Figure 3 (SEQ ID NO: 3).
- 16/37. The method of claim ¹⁴35, further comprising the step of refolding the isolated neurotrophic factor.
- 17/38. The method of claim ¹⁴35, wherein said host cell is a prokaryotic cell.
- 18/39. The method of claim ¹⁴35, wherein said host cell is a eukaryotic cell.
40. An article for treating nerve damage, comprising:
- (a) a semipermeable membrane suitable for implantation; and

09377445-081999

- (b) cells encapsulated within said membrane, wherein said cells secrete a neurotrophic factor comprising the amino acid sequence depicted in Figure 4 (SEQ ID NO: 3 or 4);

said membrane being permeable to the neurotrophic factor and impermeable to materials detrimental to said cells.

*end
p1
cont'd*

09377446.081999